UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,023	12/11/2003	Anne Vanet	1421-03	2355

35811 7590 08/06/2007
IP GROUP OF DLA PIPER US LLP
ONE LIBERTY PLACE
1650 MARKET ST, SUITE 4900
PHILADELPHIA, PA 19103

EXAMINER	
SKOWRONEK, KARLHEINZ R	
ART UNIT	**PAPER NUMBER**
1631	

MAIL DATE	DELIVERY MODE
08/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/734,023	VANET ET AL.	
	Examiner	Art Unit	
	Karlheinz R. Skowronek	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *11-19,21-27,30 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,20,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/11/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I (claims 1-10 and 20-29) and election of species of HIV protease sequences (as in claim 20), in the reply filed on 4 June 2007 is acknowledged. The traversal is on the ground(s) that the inventions of groups V-VII and VIII-X are not distinct based on the classification of groups V-VII to 530/300 and groups VIII-X to 514/2. This is not found persuasive because despite being in the same class and subclass a search for the invention of group V, drawn to a pharmaceutical composition for the treatment of influenza, for example, will not produce results reading on the invention of group VI, drawn to a pharmaceutical composition for the treatment of HIV. Similarly, a search for the invention of group VIII, drawn to a method for the treatment of influenza, will not produce results reading on the invention of group IX, drawn to a method for the treatment of HIV.

However, upon further consideration, the inventions of groups V and VIII will be rejoined as relating to influenza; the inventions of groups VI, IX will be rejoined as related to HIV; and the inventions of groups VII, X will be rejoined as being related to hepatitis C.

The requirement is still deemed proper and is therefore made FINAL.

Claims 11-19, 21-27, and 30-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4 June 2007.

Claim Status

Claims 1-31 are pending.

Claims 11-19, 21-27, 30, and 31 stand withdrawn as being directed to a non-elected invention.

Claims 1-10, 20, 28, and 29 are being examined.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 11 December 2003 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Definitions

The term "motif" has been defined by applicant to refer to a single amino acid or nucleotide with in a protein or nucleic acid sequence (specification, p. 6, [0024 and 0025]). Applicant's definition will be used to examine the claims and redefines the art-accepted definition of "motif".

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Hyperlinks can be found on pages 4 and 17.

Appropriate correction is required.

Claim Objections

Claim 6 is objected to because of the following informalities: The phrase "matrices B,C of mutations" appear to be a typographical error. The examiner suggests this objection can be overcome, an amendment to replace the phrase "matrices B,C of mutations" similar to "matrices, B and C, of mutations". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 6 is unclear with regards what the subscript variable k is. Neither the specification nor the claim provides a measure for defining the variable k.

2. Claim 6 recites the limitation "$A_{k,j}$" in line 10. There is insufficient antecedent basis for this limitation in the claim.
3. Claim 6 is unclear in line 19 in the determining step for a set of E positions, the phrase "in which i j" appears to be missing the remaining claim language.
4. Claim 6 is unclear in line 22 in the determining step for a set of F positions, the phrase "in which i j" appears to be missing the remaining language.
5. Claim 6 is unclear what the variables $C_{k,i}$ and $C_{i,k}$ are.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-20,28, and 29 are drawn to a process. A statutory process must include a step of a physical transformation, or produce a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). The instant claims do not result in a physical transformation, thus the Examiner must determine if the instant claims include a useful, concrete, and tangible result.

As noted in State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998) below, the statutory category of the claimed

subject matter is not relevant to a determination of whether the claimed subject matter produces a useful, concrete, and tangible result:

> The question of whether a claim encompasses statutory subject matter should not focus on which of the four categories of subject matter a claim is directed to -- process, machine, manufacture, or composition of matter--but rather on the essential characteristics of the subject matter, in particular, its practical utility. Section 101 specifies that statutory subject matter must also satisfy the other "conditions and requirements" of Title 35, including novelty, nonobviousness, and adequacy of disclosure and notice. See *In re Warmerdam*, 33 F.3d 1354, 1359, 31 USPQ2d 1754, 1757-58 (Fed. Cir. 1994). For purpose of our analysis, as noted above, claim 1 is directed to a machine programmed with the Hub and Spoke software and admittedly produces a "useful, concrete, and tangible result." *Alappat*, 33 F.3d at 1544, 31 USPQ2d at 1557. This renders it statutory subject matter, even if the useful result is expressed in numbers, such as price, profit, percentage, cost, or loss.

In determining if the claimed subject matter produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a claim to be "useful," the claim must produce a result that is specific, and substantial. For a claim to be "concrete," the process must have a result that is reproducible. For a claim to be "tangible," the process must produce a real world result. Furthermore, the claim must be limited only to statutory embodiments. Claims 1-20,28, and 29 do not produce a tangible result. A tangible result requires that the claim must set forth a practical application to produce a real-world result. This rejection could be overcome by amendment of the claims to recite that a result of the method is outputted to a display or a memory or another computer on a network, or to a user, or by including a physical transformation.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1-20, 28, and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In the decision of *In re* Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to use the claimed invention one of skill in the art must be able to identify either nucleotide or amino acid residues within a set of sequences that

have or have not mutated simultaneously. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The description describes comparison of sets of sequences using algorithms known in the sequence comparison art. The description does not provide detailed guidance to identify residues between sequences of set that have or not mutated simultaneously. The description does not describe methodology for determining from an alignment whether a subset of sequences the set mutated simultaneously. The disclosure does not provide guidance for identifying mutated and unmutated couples.

c) The description provides working examples of sequence comparison analysis to identify residues that differ between a query sequence and a reference sequence using an identity matrix. The description does not provide working examples of determining from an alignment, residues of a subset of sequences that mutated simultaneously. The description does not provide an example of how to mutated couples are identified

d) The nature of the invention, phylogenetic sequence comparison, is complex.

e) The prior art does not show methodology or algorithms for the determination of simultaneous mutation between sequences using sequence comparison methods. The art, at the time the invention was made, is silent regarding the timing at which mutations occur in sequences based on sequence alignment data. Rose et al. (Bioinformatics, Vol.16, No. 4, p. 400-401, 2000)

discusses the identification of hypermutations, an extreme for of mutation, in sequences. Rose et al. are silent with respect to mutations among sequences occurring simultaneously. Strimmer et al. (PNAS Vol. 94, p. 6815-6819, June 1997) discuss a method for studying the phylogenetic content of sequence alignments. While Strimmer et al. show that biological sequence data can be analyzed for phylogenetic data, they are silent on the timing of mutations, specifically if mutations occurred simultaneously. Strimmer et al. also teach that it may not always be possible to resolve the phylogenetic relationships between sequences (p. 6815, col. 2). Caride et al. (Journal of Clinical Virology, vol. 23, p. 179-189, 2002) demonstrate the method Rose et al. as applied to HIV-1 isolates and sequences of the HIV protease. Caride et al. demonstrate the hypermutability of the protease gene. Caride used phylogenetic inference to analyze sequences (figure 4). However, Caride et al. are silent with respect to mutations occurring simultaneously.

f) The skill of those in the art of phylogenetic sequence comparison is high.

g) The predictability of determining if mutations found in at least 2 sequences occurred simultaneously or not is unknown in the prior art.

h) The claims are broad in that the claims are drawn to a method of identifying residues in any sequence within a set of sequences that have mutated simultaneously with respect to at least one other sequence.

The skilled practitioner would first turn to the instant description for guidance in using the claimed invention. However, the description lacks clear

evidence of methodology for identifying at least 2 sequences in which a mutation has occurred simultaneously. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art does not discuss methods or algorithms for identifying if residues within sequences mutated simultaneously. Finally, said practitioner would turn to trial and error experimentation to determine a relationship that can be employed to elucidate markers or identifiers that indicate a mutation had occurred simultaneously in two different sequences. Such amounts to undue experimentation.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karlheinz R. Skowronek whose telephone number is (571) 272-9047. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

1 August 2007

/KRS/
Karlheinz R. Skowronek
Assistant Examiner, Art Unit 1631

J.S. Brusca 2August2007

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER